

# INTERNATIONAL SEARCH REPORT

National Application No  
PCT/US 00/19844

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>NICULESCU-DUVAZ I ET AL: "GENE-DIRECTED ENZYME PRODRUG THERAPY: A REVIEW OF ENZYME/PRODRUG COMBINATIONS" EXPERT OPINION ON INVESTIGATIONAL DRUGS,GB,ASHLEY PUBLICATIONS LTD., LONDON, vol. 6, no. 6, 1997, pages 685-703, XP000901460 ISSN: 1354-3784 schemes tables</p> <p style="text-align: center;">---</p>	1-20
Y	<p>BAGSHAW K D: "ANTIBODY-DIRECTED ENZYME PRODRUG THERAPY: A REVIEW" DRUG DEVELOPMENT RESEARCH,US,NEW YORK, NY, vol. 34, no. 2, 1 February 1995 (1995-02-01), pages 220-230, XP000562092 ISSN: 0272-4391 page 223; table 1 page 224, right-hand column, last paragraph -page 226, left-hand column</p> <p style="text-align: center;">---</p>	1-20
Y	<p>MELTON ET AL: "Antibody-directed enzyme prodrug therapy (ADEPT). Review article" DRUGS OF THE FUTURE,ES,BARCELONA, vol. 21, no. 2, 1996, pages 167-181, XP002080157 ISSN: 0377-8282 table 1 figures 2,4-9,11,13-16 page 178, paragraph CONCLUSIONS</p> <p style="text-align: center;">---</p>	1-20
Y	<p>WOLFE L A ET AL: "ANTIBODY-DIRECTED ENZYME PRODRUG THERAPY WITH THE T268G MUTANT OF HUMAN CARBOXYPEPTIDASE A1: IN VITRO AND IN VIVO STUDIES WITH PRODRUGS OF METHOTREXATE AND THE THYMIDYLATE SYNTHASE INHIBITORS GW1031 AND GW1843" BIOCONJUGATE CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY, WASHINGTON, vol. 10, no. 1, January 1999 (1999-01), pages 38-48, XP000800838 ISSN: 1043-1802 abstract figures tables</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-20

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X	<p>GRIENGL H ET AL: "PHOSPHONOFORMATE AND PHOSPHONOACETATE DERIVATIVES OF 5-SUBSTITUTED 2'DEOXYURIDINES: SYNTHESIS AND ANTIVIRAL ACTIVITY"</p> <p>JOURNAL OF MEDICINAL CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 31, no. 9, 1988, pages 1831-1839, XP002036743</p> <p>ISSN: 0022-2623</p> <p>abstract</p> <p>page 1833 -page 1834</p>	1-20
X	<p>MCGUIGAN C ET AL: "ARYL PHOSPHORAMIDATE DERIVATIVES OF D4T HAVE IMPROVED ANTI-HIV EFFICACY IN TISSUE CULTURE AND MAY ACT BY THE GENERATION OF A NOVEL INTRACELLULAR METABOLITE"</p> <p>JOURNAL OF MEDICINAL CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 39, no. 8, 1996, pages 1748-1753, XP000578130</p> <p>ISSN: 0022-2623</p> <p>abstract</p> <p>page 1748, paragraph INTRODUCTION</p> <p>table</p>	1-20
X	<p>WO 95 12678 A (CONNORS THOMAS ;KNOX RICHARD (GB); SHERWOOD ROGER (GB); CANCER RES) 11 May 1995 (1995-05-11)</p> <p>examples</p> <p>claims</p>	1-20
X,P	<p>WILDNER OLIVER ET AL: "Enzyme prodrug gene therapy: Synergistic use of the herpes simplex virus-cellular thymidine kinase/ganciclovir system and thymidylate synthase inhibitors for the treatment of colon cancer."</p> <p>CANCER RESEARCH, vol. 59, no. 20, 15 October 1999 (1999-10-15), pages 5233-5238, XP001002739</p> <p>ISSN: 0008-5472</p> <p>abstract</p> <p>figure 1</p> <p>page 5236, paragraph DISCUSSION -page 5237</p>	1-20
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KUMAR A ET AL: "SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME CYCLIC PHOSPHORAMIDATE NUCLEOSIDE DERIVATIVES" JOURNAL OF MEDICINAL CHEMISTRY, vol. 33, no. 9, 1990, pages 2368-2375, XP002171072 ISSN: 0022-2623 abstract schemes figures tables page 2371, left-hand column, last paragraph -page 2372, right-hand column, line 3 ---	1-20
Y	FARROW S N ET AL: "SYNTHESIS AND BIOLOGICAL PROPERTIES OF NOVEL PHOSPHOTRIESTERS A NEW APPROACH TO THE INTRODUCTION OF BIOLOGICALLY ACTIVE NUCLEOTIDES INTO CELLS" JOURNAL OF MEDICINAL CHEMISTRY, vol. 33, no. 5, 1990, pages 1400-1406, XP002171073 ISSN: 0022-2623 the whole document ---	1-20
P,X, L	WO 99 37753 A (GROZIAK MICHAEL P ;SHEPARD H MICHAEL (US); NEWBIOTICS INC (US)) 29 July 1999 (1999-07-29) the whole document ---	1-20
E	WO 01 07088 A (SHEPARD H MICHAEL ;NEWBIOTICS INC (US)) 1 February 2001 (2001-02-01) the whole document -----	1-20

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-20 in part

Present claims 1-20 relate to a method defined by reference to a set of desirable characteristics or properties, related to the pharmacological profile of the prodrug to be used.

The claims cover all methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only one single prodrug. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the prodrug by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Unfortunately, this lack of support, disclosure and clarity is not overcome by the structural formulae of claims 2-3.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the prodrug for which pharmacological data were provided.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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